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The use of azithromycin and fusidic acid in the treatment of mild to moderate forms of hidradenitis suppurativa

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ABSTRACT

Background: Hidradenitis suppurativa is a chronic disease with universal spread and it has a major influence on the kind of patients' life. Management should rely on the disease severity. **Objective:** We aimed to explore our experience with the use of topical fusidic acid and systemic azithromycin in mild to moderate forms of hidradenitis suppurativa (Hurley stage I and II). **Materials and methods:** A cohort study (June 2016 to June 2022) included all patients with mild or moderate forms of hidradenitis suppurativa (Hurley stage I and II). Patients with severe disease (stage III) were excluded. The outcome was measured by recurrence rate and patient satisfaction. **Results:** A-113 patients, whose mean age was 32.4± 12.1 years, were included. There was female predominance. Disease prevalence was 0.032 per 100,000 of the clinic population. The mean disease duration was 4.1± 1.5 days, not affected by gender ($p = 0.3$). In stage I, 18 (38.3%) patients excellently responded and 22 (46.8%) had a good response. Whereas, in stage II, 21 (31.8%) patients excellently responded and 29 (43.9%) had a good response. The overall response was excellent and good in 39 (34.5%) and 51 (45.1%) patients, respectively. The differences between subgroups (stages I and II) in the efficacy was statistically significant (p -value 0.001). The disease recurred in 3 (2.7%) of patients with HS, whereas it was higher in those with stage II disease. Patient satisfaction with those treated by nonsurgical means was very good / excellent in 98% of patients. **Conclusion:** The treatment regimen used was shown to be effective. Thus, they can be a first-line option for the treatment of mild to moderate conditions of hidradenitis suppurativa.

Keywords: Hidradenitis suppurativa, Acne inversa, Treatment, Management, Azithromycin, Fusidic Acid.

1. INTRODUCTION

Acne inversa or hidradenitis suppurativa (HS) is a chronic, devastating dermatological condition characterized by repeated inflammation. Lesions are nodules, deeply seated and painful, in the areas of the body that have apocrine glands, usually in the armpit, groin and anogenital regions (Hendricks et al., 2021). They can progress and lead to abscesses, sinus tracts and scars (Calao et al., 2018). To date, its precise prevalence is still obscure. Depending on the population study, its estimated prevalence varies between 0.0003% and 4% (Alsadhan et al., 2022; Napolitano et al., 2017). The emergence of the disease is ordinarily between puberty and 40 years, often between 21 and 29 years. More or less in a ratio of 3 to 1, HS tends to affect females more often (Mohammadi et al., 2021).

The diagnosis is often made by the clinical features and its chronicity depends on its usual large distribution and multi zone type of involvement. No biological or pathological test facilitates its diagnosis and a biopsy is rarely needed (Napolitano et al., 2017). Early diagnosis and treatment are crucial for the affected patients with general goals including treating existing lesions to minimize pain and drainage, reduce the frequency of recurrences and prevent the disease from progression. Since there are scarce series comparing management methods, most of the utilized treatment guidelines are based on expert opinion and consensus (Clemmensen, 1983).

Actually, HS is frequently treated by several specializations, like general surgeons, plastic surgeons and dermatologists (Calao et al., 2018). Over recent years, several HS management guidelines have been published in this era (Ingram et al., 2019; Zouboulis et al., 2019; Alikhan et al., 2019). There is little data in the literature on the use of antibiotics in the management of HS (Amat-Samaranch et al., 2021), whereas the use of azithromycin was attempted in a few studies (Melibary, 2018; Offidani et al., 2019).

Fusidic acid is an antibiotic from fusidane family. Its active ingredient has a steroid-analogous configuration but lacks steroid effect, thus not causing cross-allergies (Wilkinson, 1998). Deep within the dermis, it has a greater lowest level of inhibitory concentration (Shirah and Shirah, 2017). Its anti-bacterial properties target common skin microorganisms. It had been used to treat mild to moderate infection on the outermost cutaneous layers e.g., impetigo, intertrigo and furunculosis (Wilkinson, 1998; Shirah and Shirah, 2017), but it is used to a lesser extent in the treatment of deeper conditions such as HS, bed sores and burns (Wilkinson, 1998). Few studies have found that it is able to control HS in up to 70% of cases (Shirah and Shirah, 2017; Kamil and Affandi, 2018). In a similar way, in other studies, it was effective for treating HS, with varying and very optimistic results (Schöfer and Simonsen, 2010; Kurzen and Kurzen, 2019; Beraldo et al., 2020). For this reason, it was chosen in our practice in the management of HS.

This study was undertaken to determine the prevalence of HS and the degree of its severity and to appraise the outcome of our experience in prescribing the implemented topical and systemic antibiotics by means of disease relapse and patients' satisfaction. To our knowledge, there is no identical study in our local literature.

2. MATERIALS AND METHODS

Subjects

A cohort study from June 2016 to June 2022 included those managed by general surgeons or dermatologists in Ailmikhwah General Hospital, Al-Baha, KSA. Patients were categorized according to Hurley's classification into 3 groups; Stage I: Solitary or numerous abscesses deprived of sinus tracts and scars; Stage II: Recurring abscesses beside sinus tracts and scars; solitary/numerous broadly detached lesions; Stage III: Broad or nearly broad influence/several linked tracts and abscesses (Tchernev and Temelkova, 2019).

Stage III patients were excluded from the study. The patient was enrolled in the study one time without duplication. The patients who were originally determined as having Stage I or II HS and later on progressed to Stage III was incorporated into the category of patients suffering from stage III, so excluded from the study.

Procedure

Patients with HS stage I and II were managed by medical treatment protocol, which consisted of oral azithromycin 500 mg for 3 days (repeated weekly for 4 weeks), topical fusidic acid 20 mg ointment BID for 4 weeks, plus oral Diclofenac sodium 50 mg BID for 3 to 5 days if not contraindicated. If the patient had an abscess, it was initially incised, drained and de roofed then given the treatment regimen as above. A thorough clinical assessment and review of medical history cleared out any coexisting conditions. Candidates were advised never to utilize any additional treatments for HS.

For a minimum of 18 months, the therapy response was evaluated every four weeks. During the follow-up, patients had been evaluated by the same clinician. It was assessed how much the lesions prior to and subsequent to therapy differed. Success was determined as a more than 50% decrease in the pathological events following the course of therapy, with the proportions being excellent at more than 80%, good; between 51 and 80%, poor; between 31 and 50% and thus no response; less than 30%. For

comparison, both prior to and following treatment, photos were captured. In the last follow up patient asked about his/her satisfaction which scored from 0 to 10, when the score from 0 to 2 was considered very poor, score from 3 to 5 was poor, scores from 6 to 8 were very good and score ≥ 9 was considered excellent.

Data required

In addition to social information and medical data, medical records also contained information about the diagnosis, response to therapy, disease relapse, as well as patient satisfaction.

Data collection and management

Data was collected using a predesigned questionnaire, then distributed in a master sheet and entered into the computer. Data when entered on a personal computer were replaced with research codes, which ensured patient confidentiality. The retrieved information was utilized using SPSS version 21.0. Quantitative variables were conveyed as mean \pm SD (standard deviation), while the qualitative statistics were expressed as percentages. The relationship among the categorical data was performed using the chi-square test, where a P value lower than 0.05 was considered significant.

3. RESULTS

A-167 patients diagnosed with HS were recognized from 51491 novel patient files presented at dermatology and general surgery clinics during the study period, thus resulting in a prevalence of 0.032 per 100,000 clinic population. Their diagnosis was basically clinical. There were 54 (32.3%) patients with stage III (excluded from the study) and 113 (66.7%) patients had mild to moderate HS (47 (41.6%) stage I and 66 (58.4%) stage II). A-71 (62.8%) were female and 42 (37.2%) were male with a ratio of 1.7:1 ($p=0.02$). In view of genders, no significant dissimilarity was found in the duration of the affliction prior to the diagnosis of HS ($p=0.3$). The patient's mean age was 32.4 ± 12.1 (range, 16 – 65) years. In view of the disease pattern, the discrepancy in the disease interval before being diagnosed was statistically significant, as patients with Stage II disease were present earlier ($p=0.003$).

Generally, patients were managed as outpatients in a dermatology clinic, except those larger abscesses were managed initially as an inpatient in the surgical department with incision, drainage and de roofing, their hospitalization ranged between 0 to 2 (mean, 0.5 ± 0.7) days. The studied patient's characteristics are presented in table 1.

Table 1 Patient characteristics

N	167 patients
Male	42 (37.2%)
Female	71 (62.8%)
Male: Female ratio	1: 1.7 ($p=0.02$)
Mild to moderate HS	113 (67.7%) <div> <div>Stage I, 47 (41.6%)</div> <div>Stage II, 66 (58.4%)</div> </div>
Stage III HS	54 (32.3%), were excluded from the study
Co-incident pilonidal sinus	23 (20.4%)
Age (year)	Mean 32.4 ± 12.1 (range, 16 to 65) $p=0.3$
Duration of symptoms (days)	Mean 4.1 ± 1.5 (range, 2 to 7) $p=0.003$
Duration of analgesics (days)	Mean 2.9 ± 0.8 (range, 2 to 5) $p=0.006$
Hospital stays (days)	Mean 0.5 ± 0.7 (range, 0 to 2) $p=0.000$
Relapse and recurrence	3 (2.7%) <div> <div>Stage I: 1 (0.9%)</div> <div>Stage II: 2 (1.8%)</div> </div>

The comparative outcomes for the two subgroups (Stages I and II) are shown in table 2. In stage I, 18 (38.3%) patients excellently responded, 22 (46.8%) good responded, 4 (8.5%) poorly responded and 3 (6.4%) did not respond. In contrast, in stage II, 21 (31.8%) patients excellently responded, 29 (43.9%) good responded, 7 (10.6%) poorly responded and 9 (13.6%) did not respond. The differences between subgroups in efficiency had been tested utilizing the chi-square test and it was found to be statistically significant (p -value 0.001). Overall, the majority had an excellent and good response in 39 (34.5%) and 51 (45.1%) patients, respectively.

Table 2 Comparing outcomes between subgroups

Outcome	Subgroups		Total	P value
	Stage I	Stage II		
	Frequency (%)	Frequency (%)	Frequency (%)	
Excellent	18	21	39	0.001
More than 80%	38.3%	31.8%	34.5%	
Good	22	29	51	
Between 51 and 80%	46.8%	43.9%	45.1	
Poor	4	7	11	
Between 31 and 50%	8.5%	10.6%	9.7	
No response	3	9	12	
Less than/equal to 30%	6.4%	13.6%	10.6	
Total	47	66	113	

Recurrence of disease had been observed in 3 (2.7%) patients (Stage I: 1 (0.9%) and Stage II: 2 (1.8%)). Patient satisfaction is shown in figure 1 and table 3, It has been worthily noticeable because it was so good or excellent in 109 (96.4%) of patients with HS. However, when considering patients with abscesses, the cumulative patients' satisfaction tends to decrease as very good/excellent became 83.2%. Coincident pilonidal sinus was seen in 79 (20.2%).

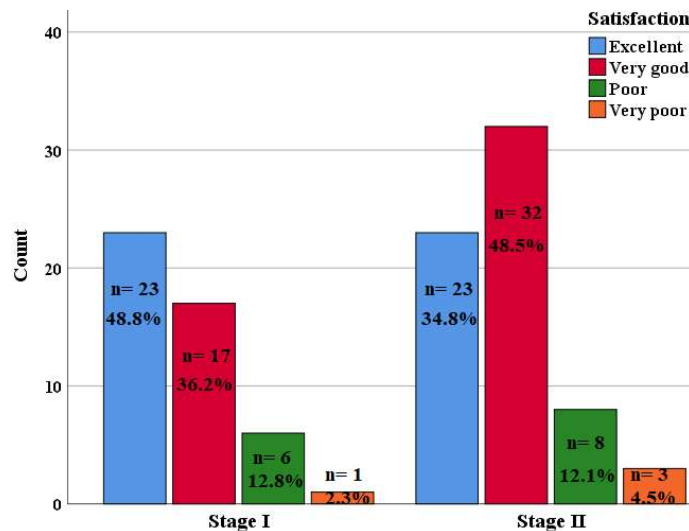

Figure 1 Overall patients' satisfaction (n=113)

Table 3 Patients' satisfaction among the study group (n=113)

Diagnosis	Very poor	Patients' satisfaction			Total	P value
		Poor	Very Good	Excellent		
Stage I	1 (2.3%)	6 (12.8%)	17 (36.2%)	23 (48.8%)	47 (41.6%)	0.8
Stage II	3 (4.5%)	8 (12.1%)	32 (48.5%)	23 (34.8%)	66 (58.4%)	
Total	4 (3.5%)	14 (12.4%)	49 (43.4%)	46 (40.7%)	113 (100%)	

4. DISCUSSION

Because of the chronic pain, drainage and foul smells associated with HS lesions, this condition possesses a significant influence on the patient's lifestyle (Patel et al., 2017). In this study, the incidence of HS was in conformity with the earliest reports in the literature, as it had been most commonly seen in females (Mohammadi et al., 2021; Wang et al., 2022; Gill and Gniadecki, 2019). It could be because females seem to be more self-aware about their appearance and consult physicians early (Darwish and Al-Rubaya, 2013). Currently, the average age of the inhabitant with HS was 32.4 years. It was less than 39 years that reported in Australia (Calao et al., 2018), but it was in concordance with others who stated that patients in their twenties are more commonly affected with the disease, while the disease is ordinarily active throughout their thirties and forties (Werth and Williams, 2000). As aesthetic

Excellency among adolescents in our region of the globe, thus research focuses on such a problem that affects youths quite frequently. The mean interval of their presenting symptoms was 65.8 days. Nevertheless, the estimated mean time lag from the commencement of symptoms among those affected till the subtle diagnosis of HS is 7.2 years (Saunte et al., 2015). Given the severe influence of HS, it is paramount to recognize its precise frequency of diagnosis as well as the prevalence, in addition to the description and peculiars of individuals affected by HS and the means of their treatment. The prevalence of HS is various and poorly explained. Aiming to demonstrate its prevalence, several studies have been undertaken in various settings and using different approaches. The prevalence of HS among presenters in this project was 0.032%, which was in agreement with others (Alsadhan et al., 2022; Napolitano et al., 2017). Saunte et al., (2015) reported little higher prevalence of 0.1% in a United States-based population. Whereas Jemec, (1988) reported a prevalence of 4 percent in females. Clinical staging and the appraisal severity of the disease are fundamental to the evolution of evidence-based management. To grade the intensity of HS, various scoring systems are available. In daily practice, comparatively all of them possess some advantages and disadvantages. Until now there is no unanimously agreed gold standard method. HS treatment choices must be affirmed by the intensity of the disease and individual subjective effects (Napolitano et al., 2017). The disease has an ample scope of clinical appearance, ranging from comparatively mild cases, recognized by the recurrent eruption of pustules, to severe form distinguished by the development of discharging sinuses, abscesses or ugly marks (Kamil and Affandi, 2018). In the current study, 67.7% of patients presented with mild disease (Stage I and II) that was treated medically whereas, the remainder 32.3% presented with severe disease (Stage III) that was excluded from the study. HS is notably hard to deal with, because of the disease diversity and it has an unpredictable course. Accordingly, any therapy in use has been adopted in accordance with the disease severity and its influence on the individual, in addition to medicine readiness and cost. Along with topical antibiotics and disinfectants, systemic antimicrobials are usually used. A combination of systemic and topical treatments might offer notable improvement; however, their complete healing effect is minimal and the recurrence rate is common (Scuderi et al., 2017). Worth noting, antibiotics were widely accepted and considered to be a first-line treatment pattern. However, routine cultures of HS lesions often identify no infection or only normal skin flora (Sakyanun et al., 2022). The choice of antibacterial treatment appears to be based primarily on personal experience or even the preference of the attending physician or the popularity of the drug administered on the favored market. Obviously, it is not given relying on microbiological cultures and sensitivity. The data in the literature are still insufficient (Matusiak et al., 2014).

While treating HS, pain management is crucial. Relying upon the disease severity and the nature of pain, topical agents and systemic non-steroidal anti-inflammatory drugs (NSAIDs) may be beneficial (Ballard and Shuman, 2019). Overall, the management of mild and moderate HS with azithromycin and fusidic acid in the current study was attributed to an excellent and good therapeutic response for the majority of patients. The rate of recurrence in the present study was 2.7% and was related to the severity of the disease, the findings were similar to that reported by others (Rompel and Petres, 2000). In the present study, using the regimen of azithromycin, fusidic acids and NSAIDs in stages I & II resulted in very good/Excellent satisfaction in 95 patients (84.1%). Information in the scholarly texts with respect to antibiotics used in the treatment of HS is limited. To the best of our knowledge, in most studies, it is recommended to either use a combination of rifampicin with clindamycin or tetracyclines (as an alternative) (Zouboulis et al., 2012), whereas others contradict their usage (Matusiak et al., 2014). The findings from our experience, propose that the use of topical fusidic acid and systemic azithromycin in stages I and II of HS is comparable.

5. CONCLUSION

HS tends to affect young females, with comparable early diagnosis. It is continuing to be a challenging disease for clinicians as well as patients. To prevent skin complications of this devastating chronic dermatological disease, it is crucial to have a precise diagnosis based on a thorough clinical examination followed by early initiation of the treatment. In general, multidisciplinary approaches that combine medical therapies and surgical management are necessary to cope with this issue. The treatment choices must be based on the severity and chronicity at the time of presentation and the experience of the physician. The use of extended systemic azithromycin and topical fusidic acid drugs plus pain control with oral diclofenac sodium was shown to be effective.

In light of the lack of existing locally based studies on the subject matter, the present study provides an opportunity to offer a solution to the management of mild to moderate stages of HS (Stages I and II), particularly when other therapies are not successful. It would necessitate additional comprehensive research to verify our findings and explore the safety profile of the two medications, which we were not able to accomplish.

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Authors' contributions

AF, FFA, SFA, SAI, HME and FSA: Conceptualized, constructed the study and gathered the data. AF, SFA, MAA, BR and FFA: Participated in data interpretation. FFA, SFA, MAA, SAI and WSA: Have written the manuscript draft. FFA, MAA, RMA, BR, HME and WSA: Revised the article and made the required amendments. AF, RMA, BR, SAI, HME and FFA: Offered scholarly subject matter of critical significance as expressed for the project. There has been unanimous approval of the final version.

Ethical considerations

The project adhered to the Declaration of Helsinki reviewed in 2000. Additionally, the proposal of the study was confirmed by the committee of research ethics, at Mikhwah General Hospital prior to conducting the study (HREC002/MGH.05/16). Written consent was obtained from the participants prior to conducting the study.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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